

Application For Research Grant

OK E
smoking study.
Date: May 25, 1955

1. Name of Investigator:

Richard L. Wechsler, M. D.

2. Title:

Clinical Physiologist

3. Institution

& Address:

Montefiore Hospital Institute of Research
3459 Fifth Ave., Pittsburgh 13, Pennsylvania

4. Project or Subject:

Effect of Cigarette Smoking on Cerebral Blood Flow, Cerebral Metabolism,
Blood Gases, Blood pH, Arterial Pulse Pressure Curves, Electrocardiograms,
and Electroencephalograms.

5. Detailed Plan of Procedure (Use reverse side if additional space is needed):

Patients or paid subjects will be chosen at random from the hospital or student population. All will be people who smoke cigarettes, but a 12 hour period of abstinence from smoking will be observed. The studies will be accomplished in the morning with the subjects in a fasting state at bed rest in the supine position. A 30 minute rest period will precede the control or "before" studies. Thirty minutes will be allotted for smoking 3 cigarettes consecutively. After finishing the last one, the experimental or "after" studies will be carried out. The following studies will be accomplished before and after smoking, and each patient will act as his own control.

1. Cerebral Blood Flow using the N_2O Technique (Kety, S.S. The Quantitative Determination of Cerebral Blood Flow in Man, Methods in Medical Research, Year Book Publishers, Chicago, 1948, Vol. I, pp 204-215.
2. Arterial and Cerebral Venous O_2 and CO_2 contents by the manometric technique of Van Slyke and Neill, (Peters, J. A. and Van Slyke, D. D., Quantitative Clinical Chemistry, Williams and Wilkins, Baltimore, 1931).
3. Arterial and Cerebral Venous pH measured anaerobically at room temperature by means of a glass electrode and Cambridge potentiometer. Values will be corrected to $37^\circ C$ by the factors of Rosenthal (Effect of Temperature on pH of Blood and Plasma in Vitro, J. Biol. Chem., 1948, 173, 25).

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BIBLIOGRAPHY

- WECHSLER, R. L., Kleiss, L. M., and Kety, S. S.: The effects of intravenously administered aminophylline on cerebral circulation and metabolism in man, *J. Clin. Invest.*, 29:28-30, January 1950. Abstract published in *Am. J. Med. Sc.*, 218-116-117, July 1949 and *Am. Heart Assoc.*, Program, 1949, pg. 55 (Presented at the Philadelphia Physiological Society Meeting, April, 1949).
- WECHSLER, R. L., Klotz, H., and Kety, S. S.: A method for estimating the uptake of P^{32} by the cellular tissues of the body in man. The effect of insulin, *Am. J. Physiol.* 159:595-596, December 1949 (Presented at the American Physiological Society Meetings, September, 1949).
- WECHSLER, R. L., Sokoloff, L. and Kety, S. S.: Measurement of hepatic circulation by clearance of radioactive sodium in man, *Federation Proceedings*, 9:467, March 1950 (Presented at the American Physiological Society Meetings, March 1950).
- WECHSLER, R. L., Dripps, R. D. and Kety, S. S.: Blood flow and oxygen consumption of the human brain during anesthesia produced by thiopental, *Anesthesiology*, 12:308-314, May 1951.
- Wechsler, L. and WECHSLER, R. L.: Phosphorus poisoning: The latent period and unusual gastrointestinal lesions, *Gastroenterology*, 17:279-283, Feb. 1951.
- Wechsler, L. and WECHSLER, R. L.: Phosphorus poisoning. (Correspondence section) *J. Am. Med. Assn.*, 147-340, 22 Sept. 1951.
- Sokoloff, L., WECHSLER, R. L., Balls, K. and Kety, S. S.: Cerebral blood flow and oxygen consumption in hyperthyroidism before and after treatment, *J. Clin. Invest.*, 32:202-208, March 1953.
- Sokoloff, L., WECHSLER, R. L., Balls, K. and Kety, S. S.: The relation of the cerebral oxygen consumption to the total body metabolism and hyperthyroidism, *J. Clin. Invest.*, 29:847, June 1950.
- King, B., Sokoloff, L., and WECHSLER, R. L.: The effects of 1-epinephrine and 1-nor-epinephrine upon cerebral circulation and metabolism in man, *J. Clin. Invest.*, 31:273-279, March 1952.
- WECHSLER, R. L.: Development of a new method for continuous measurement of cerebral blood flow in humans under acceleration. Report No. NM 001 060.03.01 Phase I of study No. NM 001 060.03 titled "Effects of Acceleration upon Cerebral Metabolism and Cerebral Blood Flow," Aviation Medical Acceleration Laboratory, Naval Air Development Center, Johnsville, Pa. August 1952.
- Duane, T. D., WECHSLER, R. L., Ziegler, J. E., and Beckman, E. L.: Studies on cerebral Physiology of monkeys at 12 negative G. Report No. NM 001 060.03.03, Phase II of Study No. NM 001 060.03 titled "Effects of Acceleration upon Cerebral Metabolism and Cerebral Blood Flow," Aviation Medical Acceleration Laboratory, Naval Air Development Center, Johnsville, Pa. *J. Av. Med.* 23:479-489, Oct. 1952, (Presented at the Aero Medical Society Meeting, 1952).

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BIBLIOGRAPHY (Cont'd)

- Sokoloff, L., King, B., and WECHSLER, R. L.: Role of 1-nor-epinephrine in the treatment of shock, Medical Clinics of North America, March, 1954.
- Sokoloff, L., WECHSLER, R. L., and Kety, S. S.: Factors contribution to the variability of the M^{24} clearance constant, American Heart Association Abstracts, 1953.
- WECHSLER, R. L., and Roth, J.: Measurement of the Rate of Gastric Emptying in Man as Determined by the Clearance of a Radioactive Colloid (AG I¹³¹): Normal Values, Effect of Urecholine Chloride and Morphine Sulfate, Federation Proceedings, 13:161, March, 1954. (Presented at the American Physiological Society Meetings, March 1954) and Am. J. Sc. (In press).
- WECHSLER, R. L., Crum, W. and Roth, J.: The Blood Flow and O₂ Consumption of the Human Brain in Hepatic Coma, Proceedings of the American Federation for Clinical Research, May 1954.
- Stone, H. H., MacKross, T. H., and WECHSLER, R. L., The Effects on Cerebral Circulation and Metabolism in Man of Acute Reduction in Blood Pressure by Means of Intravenous Hexamethonium Bromide and Head Up Tilt, Anaesthesiology, 16, 168, 1955.
- WECHSLER, R. L., Nemir, P., Meade, G., and Bellet, S., Electrocardiographic Changes following Biliary and Gastric Distention in Freshly Infarcted Unanesthetized Dogs, Surgical Forum Volume, 1954.

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Continuation of Item #5.

4. Arterial and Cerebral Venous pCO_2 will be calculated by means of the nomograms of Peters and Van Slyke, (Peters, J. A. and Van Slyke, D. D., Quantitative Clinical Chemistry, Williams and Wilkins, Baltimore, 1931).

The following studies will be accomplished at short intervals every 2 to 4 minutes before, during, and after smoking.

5. Intraarterial Pulse Pressure Wave Recordings. A Sanborn Electro-manometer and Twin Viso Recorder will be used.
6. Electrocardiograms (Standard 12 leads with multiple recordings of Lead V_4). The Twin Viso Recorder will be used.
7. Electroencephalograms with a Grass Encephalograph.

Cerebral O_2 ~~consumption~~ consumption and cerebral vascular resistance will be calculated from this data.

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Continuation of Item #8.

(3) Staff

1. Richard L. Wechsler, M.D., Clinical Physiologist, 7 years experience in field of cerebral blood flow and metabolism. (Bibliography enclosed)
2. Yale David Koskoff, M.D., Ph.D., Director of Montefiore Hospital Institute of Research.
3. Chaskiel S. Grossman, M.D., Electroencephalographer. Will read electroencephalograms.
4. Richard Abrams, Ph.D., (Biochemistry). Associate Director, Montefiore Hospital Institute of Research.
5. Mr. Philip Louis Wolf, Research Assistant, trained in techniques necessary for accomplishing project.
6. Mr. Robert Hutchison, Research Assistant, trained in techniques necessary for accomplishing project.

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6. Budget Plan:

| | |
|---------------------|-------------|
| Salaries | \$ 5,400.00 |
| Expendable Supplies | 1,600.00 |
| Permanent Equipment | 2,000.00 |
| Overhead | 1,000.00 |
| Other | |
| Total | \$10,000.00 |

7. Anticipated Duration of Work:

One Year.

8. Facilities and Staff Available:

(1) Source of Human Subjects

(2) Equipment

2 Van Slyke Manometric Gas Apparatus

1 Cambridge pH Meter

2 Grass Electroencephalographs

1 Hamilton Electromanometer (Sanborn)

1 Twin Viso Recorder (Sanborn)

Equipment for Cerebral Blood Flow Studies including gas mixtures, manifolds, syringes, and so on.

9. Additional Requirements:

None.

10. Additional Information (Including relation of work to other projects and other sources of supply):

Similar studies are in progress evaluating various anticholinergic compounds.

Signature /s./ Richard L. Wechsler
Director of Project

/s./ Yale David Koskoff, M.D.
Business Officer of the Institution

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